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PROCESS OF FORMING COLLAGEN ARTICLES AND DISPERSIONS

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This invention relates to the preparation of a colagen dispersion and the manufacture of formed collagen articles and particularly to an article of formed collagen and a process for preparing these dispersions and for forming articles such as edible sausage casings, films, tubes, casings, strands and the like from reconstituted collagen and is a continuation-in-part of my co-pending application, Serial No. 248,298, filed December 31, 1962; now abandoned. This is an improvement on application Serial No. 814,733, now U.S. Patent No. 3,071,477.

Collagen, as a naturally occurring material found in hides, bones, tendons and other animal and fish tissues, is substantially insoluble in water, but it is known that it can be rendered soluble in water by various treatments such as elevated temperature, prolonged exposure to acids, alkalis or various salts, and enzymes and bacteria and thereby be partially or completely degraded or denatured to form gelatin or other lower molecular weight polypeptides.

Collagen is a proteinaceous material which in its native state is associated with numerous other substances such as keratin, hair, elastin, mucin, reticulin, some lipids, and insoluble bound cations. Collagen in order to be useful must be separated from some of these associated materials before it can become useful in the manufacture of formed collagen articles having desirable properties.

The prior art has only recently recognized the necessity for removal of all or a portion of these non-collagenous substances, but in most cases this has not resulted in reconstituted articles with high wet strengths. For example, in one prior technique, the tissue was initially swollen in two to five percent acetic acid, then blended, as in a Waring Blendor, centrifuged, precipitated with ammonium hydroxide, washed, swollen again in acid, and then extruded (T. P. Salo, U.S. Patent 2,598,608). In a very similar technique, this entire process is essentially duplicated except that in place of blending, as by a Waring Blendor, the 2.5–5.0% acetic acid swollen collagen tissue is stirred, then diluted about five to six fold, then filtered before being neutralized by ammonium hydroxide, and then swollen in 0.6% malonic acid (E. R. Lieberman and I. B. Oneson, Canadian Patent 620,742). This last technique also duplicates a surgical sponge preparation in which tendons are sliced, swollen in 2.5% acetic acid, precipitated out by ammonium hydroxide, then swollen again in 0.6% malonic acid (R. H. Siffered and R. J. Schmitt, U.S. Patent 2,610,625). In another technique, the collagen tissue was initally swollen in acid, then coagulated and dehydrated, then alkali swollen under stress (J. P. Hollihan, Jr., U.S. Patent 2,461,602). In still another technique, a dilute acid, for example 2.5% lactic acid, is used to initially swell the collagen tissue, then the collagen fibers are tweezed out of the swollen tissue by mechanical means, and homogenized, after which additional acid, for example 0.5% lactic acid is added, before further homogenization and extrusion (W. Schulte, U.S. Patent 2,039,262). A still different process provides that the collagen tissue be treated in an alkaline medium, about pH 13, followed by acid treatment in the pH 2.5–4.0 range (Braun, U.S. Patent 2,852,812).

In Sharp Patent 1,999,641, tendons are shredded and

then carded, are defatted with organic solvents, then treated with enzymes such as lipase and tryspin at alkaline pH and then further cleaned with neutralizing agents such as sodium carbonate. A number of other techniques involve the pretreatment of various collagen containing tissue with yeast or yeast cultures or enzymes extracted from yeast followed by acid swelling (E. Rapkin, U.S. Patent 2,740,744; A. L. Lolli, U.S. Patents 2,746,949; 2,746,950; H. L. Keil, A. L. Lolli and E. F. Cavanaugh, U.S. Patent 2,751,377). It is reported that yeast and some enzyme preparations from yeast show keratinase as well as elastase activity (H. L. Keil). A number of other techniques involve the pretreatment of sliced tendon with enzyme preparations which show elastase activity, then with a chelating agent such as the tetrasodium salt of ethylenediaminetetraacetic acid to remove soluble proteins and lipids, and then with an acid in the preferred pH range of two to three (H. B. Klevens and J. Nichols, U.S. Patent 2,919,998; T. L. Reissmann and J. Nichols, U.S. Patent 2,919,999; H. R. Hochstadt and E. R. Lieberman, U.S. Patent 2,920,000).

Only a few of the most recent of the pretreatment, swelling, processing and extrusion methods mentioned above will result in reconstituted collagen articles having desirable or required properties such as wet strength. These essentially involve those pretreatments in which the enzyme systems had essentially no collagenase activity and primarily showed activity towards elastin and possibly mucin, followed by further treatments which assisted in the release of soluble proteins and lipids.

A much simpler single pretreatment step is described here which essentially involves the treatment of collagen which has not been previously treated with added enzymes with dilute solutions of various non-ionic detergents and sequestering agents. By means of this pretreatment, the concentration of lipid material and of calcium in the sliced or shredded collagen tissue is reduced and much of the soluble protein is extracted. The collagen tissue, after this pretreatment, can be treated with various swelling solutions under carefully controlled conditions of pH, temperature, time, manner of homogenization, extrusion and coagulating and/or dehydrating. Under these conditions, reconstituted collagen articles can be formed exhibiting high wet and dry tensile strengths as well as other desirable properties. Various other known adjuncts, e.g. various soluble polymeric materials and various fibers, may be added to the dispersion to impart desirable characteristics to the film. It is also possible to simply extrude and dry the film to produce a product of desirable character without the use of added coagulating agents. This treatment can be applied as a pretreatment step for any of the known methods of producing collagen dispersions and collagen films. It is, however, important that the conditions outlined in application Serial No. 814,773 be observed if the full benefit of this invention is to be achieved and the most satisfactory product obtained.

In application Serial No. 814,773 it is disclosed that the preferred process of forming a film of reconstituted collagen comprises the steps of cutting the collagen source material into finely divided pieces, treating said pieces with a solubilizing agent for calcium and other bound ions and releasing lipids, non-collagenous proteins and non-collagenous impurities from the collagen, separating the collagen mass from the released non-collagenous impurities, subjecting the remaining collagen mass to a swelling treatment in the presence of a swelling agent, shearing and homogenizing the swollen mass, controlling the temperature below about 25° C. until the swelling agent is neutralized in a subsequent dehydration step and the concentration and duration of the swelling